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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 11/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/642,218

Applicant(s)

YURIEVA ET AL.

Examiner

Richard G. Hutson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 September 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 7-10, 22, 27-29, 38-41, 44-63, 68-72 and 74-80 is/are pending in the application.
- 4a) Of the above claim(s) 55-60 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 7-10, 22, 27-29, 38-41, 44, 45, 48, 50, 52, 61, 68-72 and 74-80 is/are rejected.
- 7) ☒ Claim(s) 46, 47, 49, 51, 53, 54, 62 and 63 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants amendment of claims 7-10, 22, 28, 44, 45, 52, 61, 71, cancellation of claims 1-6, 11-21, 23-36, 30-37, 42,43,64-67and 73 and the addition of new claims 74-80 in the paper of 9/7/2004, is acknowledged. Claims 7-10, 22, 27-29, 38-41, 44-63, 68-72 and 74-80 are still at issue and are present for examination.

Election/Restrictions

Applicant's election with traverse of Group II, Claims 7-15, 22-42, 44-64 and 68-72 and Group B (i.e. the dnaX nucleic acid of SEQ ID NO: 3) in the paper of 7/28/2003 is acknowledged.

Applicants continued traversal of the previous restriction requirement is acknowledged. Applicants traversal is found persuasive in part. Specifically applicants traversal with respect to the subject matter of sub groups A and B (of Groups II as identified in paper 4) drawn to that nucleic acid encoding the tau and gamma subunits is found persuasive and those claims reading on the gamma subunit subject matter have been included in the present office action (i.e. claims 48-51)

Applicants traversal of the previous restriction requirement requesting reconsideration of sub-groups A, B, and C of Groups II is acknowledged, however, not found persuasive for the reasons previously stated.

Applicants further arguments are not found persuasive because based on the reasons previously stated and stated above it is believed that the previous

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restriction requirement is proper and necessary to ensure that the burden of search and examination of the elected invention is not so great, so as to preclude a high quality search and examination. It is believed that the additional search and examination requested by applicants would not allow for the highest quality product comprising a proper search and examination.

It is further noted that while it was not initially clear, claims 38-41 relate to the above elected subject matter, as pointed out by applicants in the previous response of 9/7/2004, and have thus been included in the current examination on the merits. Because claims 38-41 and 48-51 are newly included in the current examination on the merits, this action has been made non-final.

Claims 55-60 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Specification

The disclosure is objected to because of the following informalities:

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth: Applicants attention is drawn to the figures which contain nucleotide and/or amino acid sequences and MPEP **2422.02** -The Requirement for Exclusive Conformance; Sequences Presented in Drawing Figures

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...It should be noted, though, that when a sequence is presented in a drawing, regardless of the format or the manner of presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and the sequence identifier ("SEQ ID NO:X") must be used, either in the drawing or in the Brief Description of the Drawings.

Previously it was pointed out to applicants that figure 15 contains nucleic and/or amino acid sequences which should be described with a SEQ ID NO. as discussed above. While applicants corrected a number of sequences recited in other figures, applicants have not addressed those present in figure 15.

Appropriate correction is required.

Claim Objections

Claims 46, 47, 49, 51, 53, 54, 62 and 63 are objected to because of the following informalities:

Claims 46, 47, 49, 51, 53, 54, 62 and 63 are dependent on rejected claims.

Claims 53 and 54 are dependent on rejected claim 52.

Claims 27, 62 and 63 are directed to nonelected subject matter. (i.e. SEQ ID NOs: 87, 95 and 107).

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 10 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 remains indefinite in that it is confusing in the recitation positions 1 to 2027 of SEQ ID NO: 1" because as stated previously the sequence listing for SEQ ID NO: 1 only lists a 2007 bp sequence. Applicants amendment of figure 4B is noted, however does not help applicants overcome the rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 38-41, 44, 45, 48, 52, 61 and 68-72 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection was stated in the previous office action as it applied to previous claims 7-10, 11, 12, 22, 23, 28, 29, 30, 34, 44, 45, 52, 61 and 68-72. In response to this rejection applicants have cancelled claims 1-6, 11-21, 23-36, 30-37, 42, 43, 64-67 and 73 and amended claims 7-10, 22, 28, 44, 45, 52, 61, 71 and added new claims 74-80 and traverse the rejection as it applies to the newly amended claims 44, 45, 52, 61 and 68-72. Claims 38-41, 48, are newly included

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in the current rejection for the reasons previously stated for claims 7-10, 11, 12, 22, 23, 28, 29, 30, 34, 44, 45, 52, 61 and 68-72. Claims 38-41 will be specifically addressed after the response to applicants traversal of the original rejection.

Applicants traverse on the basis that the present application provides a nucleotide sequence and protein sequence for *Thermus thermophilus* dnaX (i.e. SEQ ID NOs: 1, 2 and 3) and that contrary to that asserted by the previous rejection applicants do identify a structural/activity relationship for tau subunits encoded by *dnaX*. Applicants submit that these are present in figures 4 and 5. Applicants further assert that the consensus "GXXGXGKT" motif for nucleotide binding is conserved in all these protein products and that this structure is related to ATP-binding.

With respect to those claims which remain in the present rejection, claims 44, 45, 52, 61 and 68-72, applicants submit that the claim language of claim 44, the independent claim is precisely the type of claim language that was acknowledged in *Univ. of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) as being acceptable under the written description requirement. Applicants submit that analogous to those claims drawn to the subgenus of "rat" cDNA encoding insulin, said to be supported by *Eli Lilly*, the currently rejected claims are supported. Applicants argument is acknowledged, however, not found persuasive because unlike the claims referred to applicants claims are drawn to any isolated DNA molecule encoding a protein subunit of DNA polymerase III-type enzyme selected from the specified groups of subunits.

There continues to be no disclosure of any particular structure to function/activity relationship in the disclosed species encompassed by the rejected claims. The specification also fails to describe additional representative species of these DNA molecules and the encoded polypeptides by any identifying structural characteristics or properties other than the type of subunit recited in the claims, for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Claims 38-41 are directed to all possible isolated DNAs which code for a recombinant DNA polymerase III-type enzyme or subunit thereof from a thermophile bacterium consisting essentially of a DNA fragment which hybridizes in a to the DNA fragments of SEQ ID NO: 6 or SEQ ID NO: 8 under the defined conditions and vectors, host cells comprising said DNA molecule and methods of use of said vector.

There is no disclosure of any particular structure to function/activity relationship in the disclosed species encompassed by the rejected claims. The specification also fails to describe additional representative species of these polynucleotides and the encoded polypeptides by any identifying structural characteristics or properties other than the activities and molecular weight, recited in the claims, for which no predictability of structure is apparent. Given

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this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 7-10, 22, 28, 29, 44, 45 and 52, 61, 68-72, and 74-80 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide encoding a τ subunit of a DNA polymerase III-type enzyme, wherein said τ subunit has an amino acid residue sequence represented by the formula shown in SEQ ID NO: 2, does not reasonably provide enablement for any polynucleotide encoding a recombinant DNA polymerase III-type enzyme or subunit thereof, from a thermophilic bacterium, consisting of a DNA which hybridizes to SEQ ID NO: 6 or 8 under the conditions defined in claim 38. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection was stated in the previous office action as it applied to previous claims 7-10, 11, 12, 22, 23, 28, 29, 30, 34, 44, 45, 52, 61 and 68-72. In response to this rejection applicants have cancelled claims 1-6, 11-21, 23-36, 30-37, 42, 43, 64-67 and 73 and amended claims 7-10, 22, 28, 44, 45, 52, 61, 71

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and added new claims 74-80 and traverse the rejection as it applies to the newly amended claims 44, 45, 52, 61 and 68-72. Claims 38-41 and newly added claims 74-80 are newly included in the current rejection for the reasons previously stated for claims 7-10, 11, 12, 22, 23, 28, 29, 30, 34, 44, 45, 52, 61 and 68-72. Claims 38-41 are included in this rejection for the same reasons previously stated for those claims previously rejected.

Applicants traverse the rejection on the basis that all that is needed is objective enablement of what is claimed and the present application provides the nucleotide sequence of a *Thermus thermophilus* dnaX (e.g., SEQ ID NOs: 1 and 3) and describes how one of ordinary skill can isolate other homologs of the disclosed sequence, and express the tau subunits and test the subunits for activity.

Applicants argue that the rejection under 35 U.S.C. §112, first paragraph is not proper because the specification teaches the complete nucleotide sequences of a *Thermus thermophilus* dnaX, protocols for using the DNA of SEQ ID NO:1 as a probe, and a protocols for testing for the encoded proteins activity. This is not persuasive because while methods to produce variants of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan producing variants as claimed by applicants (i.e., encoding a DNA polymerase type-III subunit) requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the infinite number of variants have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the

virtually infinite possibilities. This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. As previously stated the specification does not establish: (A) regions of the protein structure which may be modified without effecting τ subunit activity; (B) the general tolerance of τ subunits to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a DNA polymerase III enzyme τ subunit with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the delta subunit activity and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable, it would require undue experimentation for one skilled in the art to arrive at the majority of those DNA molecules of the claimed genus which encode a polypeptide with DNA polymerase III enzyme τ subunit activity.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any DNA

molecule from a thermophilic bacterium, encoding a DNA polymerase III-type enzyme τ subunit. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those polynucleotides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim 27 remains rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

This rejection was stated in the previous office action and repeated below for applicants convenience.

The invention of claim 27 appears to employ a novel strain of vector pET*dnaX*. Since the vector pET*dnaX* is essential to the claimed invention, it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The vector pET*dnaX* is not fully disclosed, nor has it been shown to be publicly known and freely available. The enablement requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the vector pET*dnaX*. Accordingly, it is deemed that a deposit of the vector pET*dnaX* should have been made in accordance with 37 CFR 1.801-1.809.

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Applicants traverse this rejection on the basis that the pET16b vector used by applicants remains commercially available from Novagen and the specification discloses the nucleotide sequence of a *Thermus thermophilus dnaX* and how one can insert a *Thermus thermophilus dnaX* nucleotide sequence into pET16 vector.

Applicants argument is acknowledged, however found nonpersuasive because while it is acknowledged that the parent vector pET16 was publically available and applicants teach a sequence of a *Thermus thermophilus dnaX*, applicants have not necessarily taught the sequence of that insert placed into the pET16 vector in example 3 of applicants specification. Further it appears that additional materials were necessary for the construction of pETdnaX, (i.e. pAlterdnaX, Puc19dnaXCterm as well as the amplification product generated in example3).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (571) 272-0930. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgH
11/9/2004